SUPPORT FOR THE AMENDMENTS

Claims 15-17, 20-45, and 48-73 have been canceled.

Claims 1-14, 18, 19, 46, and 47 have been amended.

Claims 74-93 have been added.

Support for the amendment of Claims 1-14, 18, 19, 46, and 47 is provided by the corresponding claims as originally filed. Support for new Claims 74-93 is provided by, for example, original Claims 1-14, 18, 19, 46, and 47. Further support for the amendment of Claim 14 is provided by Example 24.

No new matter has been added by the present amendments.

REMARKS

Claims 2-21 are pending in the present application.

In response to the Examiner's comments appearing in paragraphs 5-8 of the Office Action mailed July 29, 2008, Applicants provide the following response.

In paragraphs 5-8 of the Office Action mailed July 29, 2008, the Examiner objected to the claims as lacking unity of invention and stated that Claim 14 includes a compound disclosed in Merce-Vidal et al.

Applicant agrees in that compound [24] in Claim 14 of the present patent application was originally named incorrectly, and should instead be presented as N-[**1**-(2-diethylaminoethyl)-1H-indol-5-yl]-5-chloro-3-methylbenzo[b]thiophene-2-sulfonamide [*emphasis added*]. Applicants have amended Claim 14 accordingly to correct this error.

The name for compound [1] of Merce-Vidal et al, page 31 last paragraph is correct, namely (3-dimethylaminoethyl-1H-indol-5-yl)-5-chloro-3-methylbenzo[b]thiophene-2-sulfonamide. Thus, the compounds of the present invention (including corrected compound [24]) differ from the compounds disclosed in Merce-Vidal et al in that the indole functionality is always substituted at the 1-position with $-(CH_2)_n-R^1$ (R^1 being $-NR^8R^9$ or a nitrogen containing ring), while the indole 1-position for compounds of Merce-Vidal et al is always substituted with H, C_1-C_4 alkyl or benzyl groups. Thus, there is no overlap between both definitions.

In view of the above, sulfonamide compounds of formulae (Ia) and (Ib) of the present application are therefore not anticipated by Merce-Vidal et al. They do present a contribution over the prior art and are so linked as to form a single inventive concept within the meaning

of Rules 13.1 and 13.2 PCT. Thus, Applicants renew their request for withdrawal of the Restriction Requirement based on alleged lack of unity. An action to this effect is requested.

The rejection of Claim 14 under 35 U.S.C. §112, second paragraph, is obviated by amendment.

Compound [24] in Claim 14 of the present patent application was originally named incorrectly. Claim 14 has been corrected to provide the correct name: N-[**1**-(2-diethylaminoethyl)-1H-indol-5-yl]-5-chloro-3-methylbenzo[b]thiophene-2-sulfonamide [*emphasis added*]. Accordingly, this ground of rejection is now moot.

Withdrawal of this ground of rejection is requested.

The rejection of Claims 1-7, 9-13, 18-19, and 46-47 under 35 U.S.C. §112, second paragraph, is obviated by amendment.

Claims 1-7, 9-13, 18-19 and 46-47 have been amended to delete "preferably" phrases. Further, the claims has been amended to ensure that the phrase "optionally" or "at least" where it is used in the claims is not improperly tied to a narrower range qualified by "preferably". Accordingly, this ground of rejection is believed to be moot.

Withdrawal of this ground of rejection is requested.

The rejection of Claims 9 and 14 under 35 U.S.C. §102(b) over Merce-Vidal et al (English equivalent taken as CA 2466965) is obviated by amendment.

As stated above, Claim 14 of the present patent application was originally named incorrectly, and should instead be presented as N-[**1**-(2-diethylaminoethyl)-1H-indol-5-yl]-5-

chloro-3-methylbenzo[b]thiophene-2-sulfonamide [*emphasis added*]. Applicants have amended Claim 14 accordingly to correct this error.

The name for compound [1] of Merce-Vidal et al, page 31 last paragraph is correct, namely (3-dimethylaminoethyl-1H-indol-5-yl)-5-chloro-3-methylbenzo[b]thiophene-2-sulfonamide. Thus, the compounds of the present invention (including corrected compound [24]) differ from the compounds disclosed in Merce-Vidal et al in that the indole functionality is always substituted at the 1-position with $-(CH_2)_n-R^1$ (R^1 being $-NR^8R^9$ or a nitrogen containing ring), while the indole 1-position for compounds of Merce-Vidal et al is always substituted with H, C_1-C_4 alkyl or benzyl groups. Thus, there is no overlap between both definitions.

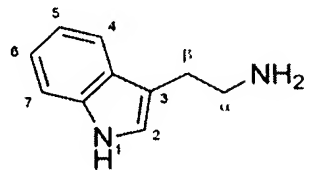
In view of the above, sulfonamide compounds of formulae (Ia) and (Ib) of the present application are therefore not anticipated by Merce-Vidal et al.

Withdrawal of this ground of rejection is requested.

The rejection of Claims 1-14, 18-19, and 46-47 under 35 U.S.C. §103(a) over Merce-Vidal et al (English equivalent taken as CA 2466965) in view of Filla et al is respectfully traversed.

Merce-Vidal et al discloses 5-HT_6 receptors, having the following substituents in the indole ring: (i) a sulfonamide in position 5; (ii) hydrogen, alkyl or benzyl in position 1 (nitrogen of the indole); and (iii) a $-(CH_2)_n-R^2$ group (R^2 being $-NR^4R^5$ or a nitrogen containing ring) at the 3-position. However, said group $-(CH_2)_n-R^2$ in the compounds of the present invention is in position 1, in this case, group $-(CH_2)_n-R^1$ (R^1 being $-NR^8R^9$ or a nitrogen containing ring).

The compounds of the present invention lack the "*tryptamine*"-like structure of the compounds disclosed in Merce-Vidal et al.

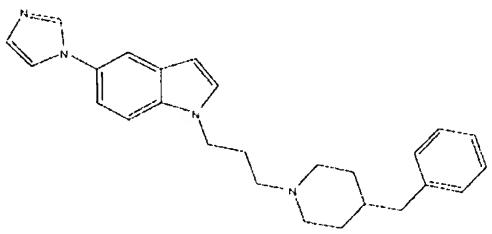


tryptamine

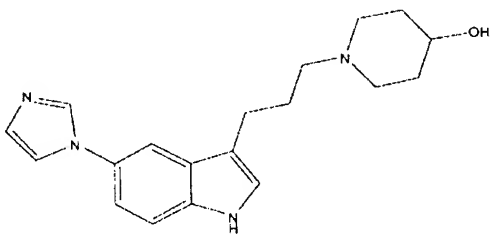
The Examiner contends that the compounds of the present invention are obvious positional isomers of the compounds disclosed in Merce-Vidal et al. According to the Examiner, the compounds of the present invention are sufficiently close to those of Merce-Vidal et al that there is a presumed expectation that they would have similar properties. Applicants respectfully disagree.

Merce-Vidal et al provides no hint as to moving the amino moiety or the *N*-containing cycloaliphatic ring to the 1-position of the indole ring without losing affinity for the 5-HT_6 receptor.

In addition, the Examiner's assertions do not stand comparison with similar situations described in the state of the art. For example, compound (1) is claimed as inhibitor of thromboxane A2 synthesis in WO 9320065, while compound (2), having a similar substituent but in position 3, is described as highly selective h5-HT1D receptor agonist in Russell, M.G.; *J. Med. Chem.*; (**1999**); 42(24); 4981-5001.

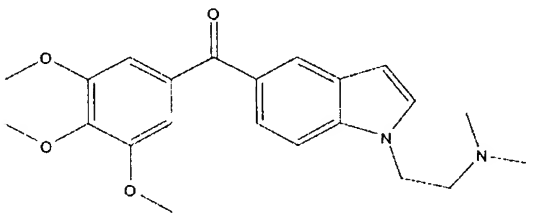


Compound (1)

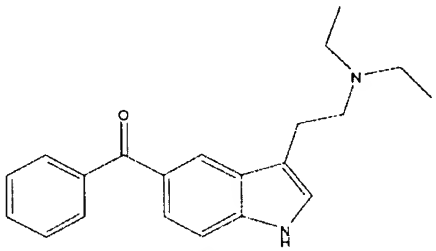


Compound (2)

A similar situation arises when comparing compound (5), which is described as potent antitubulin agent in Liou, J.P.; *J. Med. Chem.*; (**2007**); 50(18); 4548-4552, with compound (6) of Leonard, B.E.; *Neuropharmacology*; (**1972**); 11(3); 373-384, which is described as having effects on brain monoamines and their precursor amino acids.



Compound (5)



Compound (6)

Thus, the skilled artisan when considering Merce-Vidal et al in light of the prior art, could expect changing the $-(CH_2)_n-R^2$ moiety to position 1 to have dramatic changes in the properties of the resulting compounds.

Moreover, the skilled artisan would not have been motivated to change the $-(CH_2)_n-R^2$ moiety of Merce-Vidal et al to position 1 in view of the disclosure of Filla et al (WO'871). Both compounds mentioned by the Examiner (Example 28 and Example 29) would be more related to compounds disclosed in Merce-Vidal et al, and not at all related with the compounds of the present invention. Both compounds are substituted in position 1 by an alkyl group (pro-1-yl and cyclopentyl, respectively). None of them is substituted in position 1 by the $-(CH_2)_n-R^1$ (R^1 being $-NR^8R^9$ or a nitrogen containing ring) characteristic of the compounds of the present invention. Thus, no motivation can be deduced to provide the compounds of the present invention from the fact that Filla et al reports two compounds possibly more related to Merce-Vidal et al could have similar biological activities.

Even if Filla et al reported a compound related to the present invention, i.e. a compound wherein the position 1 of an indol ring is substituted by a $-(CH_2)_n-R^1$ (R^1 being –

NR^8R^9 or a nitrogen containing ring), the applicant has already explained how the prior art shows that the positional isomers could also be expected to have very different activities.

Further, at the date of filing, Filla et al did not contain any experimental data about the biological activity of the compounds described therein. Although, Filla et al describes how *in vitro* tests could be carried out, no results at all are mentioned. Thus, at the filing date of the present application Filla et al did not disclose any information at all regarding possible biological activities of positional isomers.

Thus, the skilled person in view of Merce-Vidal et al in combination with Filla et al would not expect the compounds of the present invention to have similar activity.

Applicants further submit that Merce-Vidal et al fail to provide any disclosure or suggestion of how their compounds may be or should be modified to arrive at the claimed compounds. To this end, Applicants direct the Examiner to *Takeda Chemical Industries Ltd. v. Alphapharm Pty. Ltd.*, 83 USPQ2d 1169 (Fed. Cir. 2007) in which the Court of Appeals for the Federal Circuit clearly state that in order to find a *prima facie* case of unpatentability, a showing that the "prior art would have suggested making the specific molecular modifications necessary to achieve the claimed invention" was also required (*Takeda* at 1174, citing *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992); *In re Dillon*, 919 F.2d 688, 16 USPQ2d 1897 (Fed. Cir. 1990); *In re Grabiak*, 769 F.2d 729, 226 USPQ 870 (Fed. Cir. 1985); *In re Lalu*, 747 F.2d 703, 223 USPQ 1257 (Fed. Cir. 1984)).

Moreover, as clearly stated by *Takeda* at 1174, the Court squarely addressed the test for *prima facie* obviousness enunciated by the Supreme Court in *KSR International Co. v. Teleflex Inc.*, 127 S. Ct. 1727 [82 USPQ2d 1385](2007) in the context of chemical compounds:

> That test for *prima facie* obviousness for chemical compounds is consistent with the legal principles enunciated in *KSR*.[2] While the *KSR*

> Court rejected a rigid application of the teaching, suggestion, or motivation("TSM") test in an obviousness inquiry, the Court acknowledged the importance of identifying "a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does" in an obviousness determination. *KSR*, 127 S. Ct. at 1731. Moreover, the Court indicated that there is "no necessary inconsistency between the idea underlying the TSM test and the *Graham* analysis." *Id.* As long as the test is not applied as a "rigid and mandatory" formula, that test can provide "helpful insight"to an obviousness inquiry. *Id.* Thus, ***in cases involving new chemical compounds, it remains necessary to identify some reason that would have led a chemist to modify a known compound in a particular manner to establish prima facie obviousness of a new claimed compound.*** (*emphasis added*)

In view of the foregoing, Applicants submit that the present invention is not obvious in view of Merce-Vidal et al as this reference fails to provide the requisite reason that would have led a chemist to modify the compounds disclosed therein in the manner necessary to arrive at the claimed compounds. Thus, Merce-Vidal et al fails to support even a *prima facie* case of obviousness.

In view of the foregoing, Applicants request withdrawal of this ground of rejection.

The provisional obviousness-type double patenting rejections of Claims 1-14, 18, and 46 over (a) copending US 10/566,101 in view of Laconde et al and (b) copending US 10/566,403 in view of Laconde et al, are requested to be held in abeyance until a determination of the scope of allowable subject matter has been obtained in the present application. At that time, if necessary, a Terminal Disclaimer may be filed. Until such a time, Applicants make no statement with respect to the propriety of these grounds of rejection.

Applicants submit that the present application is now in condition for allowance.

Early notification of such action is earnestly solicited.

Respectfully submitted,

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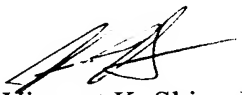
MAIER & NEUSTADT, P.C.
Norman F. Oblon



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